Exhibit 5

EXPERT REPORT OF MARK A. SCHUMACHER, M.D., Ph.D.

MARCH 25, 2019

I. INTRODUCTION

1. My name is Mark A. Schumacher, M.D., Ph.D. I have been retained by Plaintiffs Cuyahoga County and Summit County to offer my expert opinions on issues related to the medical use of opioids for the treatment of pain, the conduct of opioid manufacturers relating to the marketing and promotion of prescription opioids, and related topics.

2. My curriculum vitae, a copy of which is attached as **Appendix 1** to this report, describes my education, background, qualifications, and my publications. I have not testified in deposition or at trial in the last four years.

3. I am being compensated at a rate of $450 per hour for my services in this litigation. I am also being reimbursed for all reasonable expenses incurred for my work on this litigation. No part of my compensation is contingent upon the outcome of this litigation, and I have no interest in the litigation or with either party.

4. This report contains a true and accurate statement of my opinions in this matter. The matters cited in this expert report are based on my personal knowledge, education, and years of medical experience and, if called to testify, I will testify to the same effect. These opinions are based on my education, training and experience as well as the data, evidence, and literature cited herein and are offered to a reasonable degree of medical certainty. I reserve the right to supplement my analysis and opinions based on additional evidence or information that is made available to me after the date of this report, including additional expert disclosures made after March 25, 2019, as approved by the Court.

II. SUMMARY OF OPINIONS:

5. It is my opinion, based on my expertise in the field of pain management, that the increased prescribing of opioids in the United States has caused tremendous harm that would not have occurred if not for the actions of the companies that aggressively promoted the use of

opioids for a wide array of conditions beyond short-term acute pain, cancer pain from active disease, and end-of-life and hospice care.

6. The prevalence of chronic pain is a valid concern but should not be confused with underutilization of opioids. In addition, to the extent that there was some amount of under-treated pain, it does not follow that the best treatment then (or now) would have been an opioid; indeed, in the vast majority of cases the best treatment would have been something other than an opioid, and likely a combination of physical, pharmacologic, and behavioral approaches.

7. More specifically, I provide the following opinions based on my experience, review of academic literature, and review of documents and certain information produced in discovery in this action:

8. It is my opinion to a reasonable degree of certainty in the field of pain medicine that the medical standard of care for treating both chronic and acute pain was changed as a result of widespread promotion and marketing of opioids by Defendants[1] that trivialized the risk of addiction and exaggerated the benefits of long-term opioid use.

9. It is my opinion to a reasonable degree of certainty in the field of pain medicine that Defendants influenced physicians through direct-to-physician marketing, medical education, and industry-sponsored and -funded Key Opinion Leaders ("KOLs") to prescribe long-term opioids based on misinformation about the risks and benefits of chronic opioid use.

10. It is my opinion to a reasonable degree of certainty in the field of pain medicine that for the vast majority of chronic pain patients, the risks of prescription opioids significantly

[1] "Defendants" as used herein refers to the Defendant manufacturers of branded and generic opioid products in the actions brought by Plaintiffs Cuyahoga County and Summit County: Purdue Pharma, Endo, Janssen, Teva, Cephalon, Mallinckrodt, Actavis, and Allergan.

outweigh any benefits, and that at most, a small percentage of chronic pain patients achieve meaningful relief from the long-term use of opioids.

11. It is my opinion to a reasonable degree of certainty in the field of pain medicine that even for those indications for which opioids are effective, such as trauma or post-operative pain, the risks of prescribing opioids are significant such that non-opioid alternatives or multimodal analgesia should be used whenever possible to reduce opioid use.

III. BACKGROUND

A. General qualifications and background

12. I am a Professor and Chief of the Division of Pain Medicine in the Department of Anesthesia and Perioperative Care, University of California, San Francisco (UCSF). My education and training include a PhD (Physiology and Pharmacology) and M.D. at the University of California, San Diego. Following an internal medicine internship at Cedars Sinai Medical Center, I completed a residency in anesthesiology at UCSF and devoted my academic career to advance pain medicine through clinical care, teaching and research. I advanced Clinical Pain care at UCSF through the introduction of low-dose ketamine, a non-opioid analgesic adjunct that decreases opioid tolerance, opioid requirements and reduces hyperalgesia (Anesthesia & Analgesia 2001); introduced multimodal analgesia for orthopedic joint surgery to minimize opioids and enhance early mobilization and discharge; served as Director of UCSF Pain Services 2010-2015 and am currently serving as Chief of Pain Medicine since 2010; and directed three UCSF Pain Summits (2011, 2013, 2015). I also served on the National Academies of Sciences, Engineering, and Medicine, Committee on Pain Management and Regulatory Strategies to Address Prescription Opioid Abuse - Consensus Report, July 2017: "Pain Management and the Opioid Epidemic" (R. Bonnie 2017).

treatment of pain, to the market forces that caused a decrease in the availability of multidisciplinary pain treatment—there is no real question that the epidemic has been driven by an unwarranted increase in prescription opioids orchestrated by the pharmaceutical industry. The total opioid prescribing rate more than doubled in the U.S. from 1995 to 2013 (IMS Health 1997-2013). This trend is confirmed by prescription data from 1995-2010 derived from the National Ambulatory Medical Care Survey showing a substantial increase in opioid prescriptions between 1995 and 2010 in office-based medical visits, especially in visits by middle-aged and older adults and by patients making their first visit to the treating physician (Olfson et al. 2013).

A. The medical standard of care for treating both chronic and acute pain was changed because of widespread promotion and marketing of opioids that trivialized the risk of addiction and exaggerated the benefits of long-term opioid use.

55. As part of our work on the NASEM Consensus Study Report, my colleagues and I relied on a traditional multi-factorial causal model commonly used in public health, ranging from structural factors to individual susceptibility. Using this approach, we found certain hypotheses about "causes" of the epidemic to be inescapable. Of particular note, data present a prima facie case that heavy promotion of opioid prescribing by Defendants (including misleading claims), substantially increased prescribing by physicians and was the key contributor to the increase in misuse, OUD, and accompanying harms. (Van Zee 2009; GAO 2003; Hoffman 2016; Cicero, Inciardi, and Munoz 2005; 'Vital signs: overdoses of prescription opioid pain relievers - United States, 1999-2008' 2011).

56. Opioid manufacturers took advantage of physicians' desire to provide relief to large population of people with chronic pain conditions. In 2016, the CDC estimated 50 million US adults suffer chronic pain, defined as reporting pain every day or most days over the past 6 months; and 19.6 million U.S. adults suffer from "high-impact chronic pain," defined as chronic pain that frequently limits life or work activities (Dahlhamer et al. 2018). The CDC explains:

"National estimates of high-impact chronic pain can help differentiate persons with limitations in major life domains, including work, social, recreational, and self-care activities from those who maintain normal life activities despite chronic pain, providing a better understanding of the population in need of pain services." (Dahlhamer et al. 2018) Chronic pain, however, is complex and difficult to treat.

57. While multidisciplinary pain treatment demonstrates substantial effectiveness, for the reasons discussed above, access to this type of treatment diminished in the 1990s. Yet, of course, physicians' desire to help their patients remained. It is, thus, particularly unfortunate from a public health perspective that it was at this precise moment that Purdue's unprecedented marketing campaign for OxyContin took shape (GAO 2003). It was fertile ground for a campaign based on the promise that these opioids were new and improved and specifically designed to provide effective relief for chronic pain with very low risk of addiction.

1. The campaign to persuade doctors to prescribe "new" opioids

58. In my opinion, the driving force of this national catastrophe has been the introduction and marketing of long-acting formulations of high potency opioids such as OxyContin beginning in 1996. Physicians were misled through Defendants' marketing and sales detailing intended to persuade doctors to accept that more potent and long-acting formulations of opioids (such as OxyContin) were safe and effective in the treatment of multiple forms of pain, especially chronic non-cancer pain, and even at high doses.

59. Purdue and other Defendants utilized a number of approaches to encourage physicians to prescribe opioids broadly for the treatment of chronic pain. They engaged in direct-to-consumer marketing. They marketed directly to physicians through sales representatives. They funded research, pain-related medical societies, and continuing medical education, lobbied medical boards and agencies responsible for pain-related treatment guidelines,

and lobbied state and local government to remove barriers to broader use of opioids for the treatment of pain. ('Fueling an epidemic. Exposing the financial ties between opioid manufacturers and third party advocacy groups' 2018). A common feature across all of these efforts to promote the broader use of opioids was the message that the risk of addiction was rare, and the benefits of long-term opioid use were well established. These efforts were remarkably successful:

> An in-depth analysis of the promotion and marketing of OxyContin (Purdue Pharma, Stamford, CT), a sustained-release oxycodone preparation, illustrates some of the key issues. … OxyContin's commercial success did not depend on the merits of the drug compared with other available opioid preparations. The *Medical Letter on Drugs and Therapeutics* concluded in 2001 that oxycodone offered no advantage over appropriate doses of other potent opioids. Randomized double-blind studies comparing OxyContin given every 12 hours with immediate-release oxycodone given 4 times daily showed comparable efficacy and safety for use with chronic back pain and cancer-related pain. … In 2001 alone, the company spent $200 million in an array of approaches to market and promote OxyContin.
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> From 1996 to 2001, Purdue conducted more than 40 national pain-management and speaker-training conferences… Purdue promoted among primary care physicians a more liberal use of opioids, particularly sustained-release opioids. …
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> Purdue's promotion of OxyContin for the treatment of non–cancer-related pain contributed to a nearly tenfold increase in OxyContin prescriptions for this type of pain, from about 670 000 in 1997 to about 6.2 million in 2002… Prospective, randomized, controlled trials lasting at least 4 weeks that evaluated the use of opioids for chronic, non–cancer-related pain showed no consistent improvement in physical functioning. …
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> When OxyContin entered the market in 1996, the FDA approved its original label, which stated that iatrogenic addiction was "very rare" if opioids were legitimately used in the management of pain. In July 2001, to reflect the available scientific evidence, the label was modified to state that data were not available for establishing the true incidence of addiction in chronic-pain patients [and] also deleted the original statement that the delayed absorption of OxyContin was believed to reduce the abuse liability of the drug.
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> …Purdue funded more than 20 000 pain-related educational programs through direct sponsorship or financial grants, providing a venue that had enormous influence on physicians' prescribing throughout the country.

(Van Zee 2009). Evidence I have reviewed, including Defendants' internal communications, sales representative training materials and call notes, and promotional materials supports Dr. Van Zee's conclusions. A number of examples of this information are attached to my report as Exhibits A-C. These examples are not intended to be exhaustive, but, rather, illustrative of the Defendants' actions.

60. It is my opinion that as a result of direct-to-consumer and direct-to-physician marketing, as well as other efforts by opioid manufacturers to promote the widespread and long-term use of opioids, that the risk of addiction was trivialized, and the benefits of long-term opioid use overstated. Physicians were influenced by these efforts and a cautious and conservative approach to the use of opioids for the treatment of pain was replaced with much more liberal prescribing practices. I observed this firsthand in my own training after emerging from residency in 1995 to find increasing use of more potent formulations of opioids and sustained-release opioids for acute and chronic noncancer pain.

2. Specific misstatements designed to encourage physicians to overcome their reluctance to prescribe opioids liberally for chronic pain

61. Opioid manufacturers promoted chronic use of opioids based upon a set of key misrepresentations. These included the following: (1) taking long-acting opioids as prescribed for pain protects against addiction and abuse; (2) that new opioid formulations had no ceiling dose and were safe at high doses; and that (3) chronic opioid therapy improves function and quality of life. These misrepresentations appeared in print promotional materials and were also repeated by sales representatives in their direct marketing to physicians. In addition, (4) Purdue, at OxyContin's launch, took advantage of and was careful to maintain the perception that oxycodone is less potent than morphine, when in fact it is more potent.

a. Opioid manufacturers claimed taking long-acting opioids as prescribed for pain protects against addiction and abuse.

62. As discussed above, in 1996 when OxyContin was released, physicians generally were reluctant to prescribe opioids on a long-term basis because of fears of addiction. Purdue, of course, knew this through market studies that demonstrated this concern. Purdue admitted this when it pled guilty in 2007 to misbranding OxyContin:

> During the period February through March l995, PURDUE supervisors and employees obtained market research that included focus groups of forty primary care physicians, rheumatologists, and surgeons to determine their receptivity to using OxyContin for non-cancer pain. According to this market research, some of these physicians had concerns, similar to their concerns about combination opioids, regarding OxyContin's addictive potential and side effect profile, including that "[t]he biggest negative of [OxyContin] was the abuse potential."

See Agreed Statement of Facts, *United States. v. Purdue Frederick Co.*, No. 1:07-cr-00029 (W.D. Va. May 10, 2007) ("Purdue Guilty Plea") at §19. Internal documents produced in discovery confirm Purdue's knowledge of physicians' reluctance to prescribe opioids for non-cancer pain. *See* Exhibit C. For example, notes from a June 9-11, 1995 OxyContin Investigators' Meeting indicate that "among health care providers there is a perception that patients feel a 'stigma' associated with opioid analgesic therapy. Morphine and hydromorphone are most associated with this stigma. One of the patients' biggest fears appears to be the possibility of addiction…" PKY181823986 at 17 (*See* Exhibit C-2).

63. Sales representatives used multiple approaches to persuade physicians who expressed caution and concerns about the abuse and addiction potential of oxycodone and OxyContin. *See* Exhibit A. This amounted to repeated falsehoods that OxyContin / oxycodone had a decreased potential for addiction, was superior to and a less addictive alternate than combination forms of opioid analgesics containing hydrocodone (equal potency to morphine)

> Oxycodone has a 'personality' that is influenced by many years of oxycodone use in Percocet. We have built a large part of our platform on this personality and used it to differentiate OxyContin from MS Contin and .... This differentiation has lead [sic] to much non-malignant business. Marketing is not only about what you are. It is also about what you are not. We have a success beyond our expectations that is, in part, due to the unique personality of OxyContin.

PPLP004030162 at p. 1 (Exhibit C-9). Purdue admitted that it was "well aware of the incorrect view held by many physicians that oxycodone was weaker than morphine" and "did not want to do anything 'to make physicians think that oxycodone was stronger or equal to morphine.'" Purdue Guilty Plea at ¶29. Similarly, and as noted above, Purdue was careful not to describe OxyContin in any way that suggested that it was as strong as morphine – when in fact, it was stronger. Examples of this are provided in Exhibit C, including:

- Email from M. Cullen, June 2, 1997, PPLP004032323 at p. 4 (Exhibit C-6) ("Since the non-cancer pain market is much greater than the cancer pain market, it is important that we allow this product to be positioned where it currently is in the physician's mind. If we stress the "Power of OxyContin" versus morphine, it may help us in the smaller cancer pain market, but hurt us in the larger potential non-cancer pain market. Some physicians may start positioning this product where morphine is used, and wait until pain is severe before using it…. It is important that we not change the position perception of physicians towards oxycodone when developing promotional pieces, symposia, review articles, etc..").

- Friedman Email to R. Sackler, May 28, 1997, PPLP004030150 at 1 (Exhibit C-5 at 5) ("it would be extremely dangerous, at this stage in the life of this product, to tamper with this 'personality,' to make physicians think the drug is stronger or equal to morphine.").

80. Doctors were reluctant to prescribe morphine for chronic pain because they understood the risk of abuse and addiction. By perpetuating confusion regarding the strength of oxycodone, and the purportedly less-addictive attributes of the extended-release mechanism, Purdue changed prescribing practices.

B. Opioid manufacturers took advantage of their ability to influence physicians through direct-to-physician marketing, medical education, and industry-sponsored and -funded KOLs.

81. Opioid manufacturers took advantage of physicians' desire to provide relief to the large population of people with chronic pain conditions. Chronic pain is complex and difficult to treat. While multidisciplinary pain treatment demonstrative substantial effectiveness, for the reasons discussed above, access to this type of treatment diminished in the 1990s. Yet, of course, physicians' desire to help their patients remained. It is, thus, particularly unfortunate from a public health perspective that it was at this precise moment that Purdue's unprecedented marketing campaign for OxyContin took shape. It was fertile ground for a campaign based on the promise that this opioid was new and improved and specifically designed to provide effective relief for chronic pain with very low risk of addiction.

82. Studies show that detailing is effective.[4] In addition, KOLs and mentors play a significant role educating physicians. They are highly influential, they are trusted – when a department head, or well-known and prominent academic physician says this is how you treat this condition, doctors follow suit. Residency is hierarchical; residents are students who learn from their seniors, like an apprenticeship. And when presented with studies supporting the view of the KOLs – that is influential, too.

83. Although it is unknown precisely the depth of the influence opioid-related industries such as Purdue may have had on academics, published literature and their influence on

[4] See e.g., Datta A and Dave D. Effects of Physician-directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence. Health Economics. April 2017;26(4):450-469; Stros M and Lee N. Marketing dimensions in the prescription pharmaceutical industry: a systematic literature review. J of Strategic Marketing 2015;23(4):318-336; Anon. Persuading the Prescribers: Pharmaceutical Marketing and its Influence on Physicians and Patients. November 11, 2013. http://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2013/11/11/persuading-the-prescribers-pharmaceutical-industry-marketing-and-its-influence-on-physicians-and-patients Accessed August 13, 2018; Gonul, F., Carter, F., Petrova, E., & Srinivasan, K. (2001). Promotion of prescription drugs and its impact on physicians' choice behavior. Journal of Marketing, 65, 79–90.

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faculty as Key Opinion Leaders, the failure to disclose industry-academic relationships is insidious and has undoubtedly impacted the practice of a generation of providers and trainees (Fauber 2011a). When confronted with conflict of interest, some academic centers have curtailed their relationships with these industries (Fauber 2011b).

84. These and other forces were brought to bear on providers both in private practice and academics and I believe exerted a strong influence. As a result, the standard of care was changed across the country. Compounding the problem was the limits of medical education on how to treat pain generally, and especially chronic pain. There is no common pain management curriculum that is broadly utilized for US medical, dental, pharmacy, or nursing schools that would be of similar rigor as, for example, the evaluation and treatment of chest pain. As of 2010, a survey of 117 US and Canadian medical schools concluded that pain curriculum was limited in time and scope (Mezei and Murinson 2011).

85. Although the majority of medical schools contain some pain curriculum, it is primarily embedded in other core course structures and is not generally regarded as a stand-alone topic. Alternately, much of pain management has been taught on the wards from senior to junior trainees. In 2010, the National Institutes of Health (NIH) Pain Consortium held a workshop on the state of pain education in the United States—overall there was inadequate education and training in pain management across the country. Opioid manufacturers took advantage of this education vacuum. Through the message that doctors could provide chronic pain relief to their patients, with simply the administration of OxyContin every 12 hours, and with very effective messengers—both drug representatives and prominent medical leaders in the field of pain management—the standard of care for treating pain was changed.[5]

[5] The fact that detailing is proven to be highly effective means that it has the potential to influence provider practice, and it has also been shown to be effective prescriber education outside of the sales context, with what is referred to

C. For the vast majority of chronic pain patients, the risks of prescription opioids significantly outweigh any benefits, and that at most, a small percentage of chronic pain patients achieve meaningful relief from the long-term use of opioids

86. At most, opioids are properly indicated for the short-term treatment of severe acute pain (e.g. trauma or post-surgical pain); end-of-life pain/hospice care; and cancer pain from active malignant disease. Chronic opioid therapy is not recommended for most common chronic pain conditions, including low back pain, centralized pain such as fibromyalgia, and headache pain. In less common chronic pain conditions (such as pain from advanced multiple sclerosis, sickle cell disease, pain following spinal cord injury and paraplegia, or post-herpetic neuralgia), which comprise a small percentage of chronic pain patients, opioids may be considered a third-line therapy (taken if other therapies are ineffective or contraindicated) for moderate and severe pain. However, in other neurologic conditions such as polyneuropathy, no functional status markers were improved by long-term use of opioids, adverse outcomes were more common among patients with polyneuropathy receiving long-term opioids, including depression opioid dependence and opioid overdose (Hoffman et al. 2017).

87. In addition to diagnosis, clinicians should consider risk, and some patients may not be suitable candidates on the basis of that risk.

88. Given the narrow categories that may indicate opioids for chronic use, opioids' position as third-line therapy, and the significant risks associated with its use, long-term opioid therapy for persons with chronic pain conditions is, at most, indicated in fewer than 5% of patients with chronic pain and likely significantly fewer, as explained below.

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as "academic detailing" or sometimes "systems consultation." See Avorn J, Soumerai SB. Improving drug therapy decisions through educational outreach. A randomized controlled trial of academically based "detailing." N Engl J Med 1983; 308:1457-1463. As providers search for professional guidance in applying emerging evidence to their opioid prescribing practices, such educational detailing from trusted colleagues will be critical to separate fact from fiction among the pervasive marketing environment that surrounds the current practice of medicine in the United States.

89. For all proper indications other than terminal cancer, palliative care and hospice care, if prescribed, opioids should be prescribed with the lowest effective dose of immediate-release opioids taken only when needed.

1. Opioids are not recommended for most common chronic pain conditions.

90. The use of opioids for the management of chronic pain represents the rationale for the prescribing of a large percentage of overall opioid medication consumed each year in the United States. Common types of pain for which these drugs are prescribed include back pain, arthritis, and neuropathic pain (e.g., pain involving tissue injury). Yet there is only minimal evidence of effectiveness of opioids for successful management of chronic pain from rigorous studies lasting more than 6 weeks (Chou et al. 2015). Amongst the complications now associated with the chronic use of opioids for pain are withdrawal, dependence, tolerance, hyperalgesia, diversion, misuse, abuse, addiction, hypogonadism (specifically low testosterone in men, and amenorrhea/dysmenorrhea in women), falls, fractures, sleep-disordered breathing, increased pain after surgery, and poorer surgical outcomes, immunosuppression, and increases in feeding and growth hormone that can lead to weight gain. (Baldini, Von Korff, and Lin 2012; Chou et al. 2015).

91. In the case of the most common chronic pain conditions, including low back pain, centralized pain such as fibromyalgia, and headache pain, patients have better outcomes if opioid treatment is avoided. These conditions together comprise the vast majority of chronic pain complaints, with low back pain being the most commonly reported chronic pain condition. (Henschke, Kamper, and Maher 2015; Breivik et al. 2006; Gran 2003; Freburger et al. 2009).

92. Several meta-analyses examine the efficacy of opioids in specific pain conditions such as neuropathic (Gaskell et al. 2016; McNicol, Midbari, and Eisenberg 2013) and back pain (Abdel Shaheed et al. 2016; Chaparro et al. 2014). Additional analyses have included